PATENT
Attorney Docket **061567-5001**

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: **Andrew Howard *et al.***

Application No. **09/914,106**

Filed: **August 23, 2001**

Group Art Unit: **1646**

Examiner: **Michael D. Pak**

For: **G Protein-Coupled Receptor Resembling Galanin Receptors**

DECLARATION UNDER 37 C.F.R. 1.132

I, Brian O'Dowd, do hereby make the following declaration:

1. I am an inventor in the above-referenced application.

2. I have reviewed the Office Action dated October 18, 2005 in the above-referenced application, in particular the Examiner's comments concerning the rejection under 35 U.S.C. 101 for the purported lack of either a specific and substantial asserted utility or a well established utility for the invention set forth in claims 14 to 34.

3. The nucleic acid molecule in claims 14 to 34 (SEQ ID NO: 1) encodes the GPR54 gene which is a G-protein-coupled receptor and this receptor is expressed in brain (see Figures 6 and 7). In the specification of the above referenced application, it is stated that agonists and antagonists of the GPR54 receptor are useful in the treatment of sexual disorders (see page 24, line 25). The specification also discloses that gene therapy may be used to introduce DNA encoding GPR54 into the cells of target organs and that this procedure would be useful for the treatment of diseases where it is beneficial to elevate GPR54 activity (see page 28, line 9 to 20).

4. Applicants submit herewith a peer-reviewed journal publication (Seminara *et al.* (2003) attached as Exhibit A) published after the filing date of the present application which supports the role of the GPR54 gene in sexual disorders. This publication demonstrates that the GPR54 receptor is a regulator of puberty, and that mutations in GPR54 gene caused the sexual disorder hypogonadotropic

hypogonadism in humans (see Figure 1 and "Conclusions" on page 1614). Seminara *et al.* disclose that transgenic mice lacking the GPR54 receptor were produced which failed to undergo puberty and mutant males were sterile with very small genitalia (see Figure 5). Mutant female mice also failed to undergo sexual maturation and failed to conceive when paired with fertile males. These females do not progress through the oestrus cycle (see page 1622, first column, third paragraph). These animal studies indicate that the GPR54 receptor is required for a subject to undergo puberty.

5. Applicants also submit herewith a second a peer-reviewed journal publication (Semple *et al.* (2005) attached as Exhibit B) which also identifies mutations in the GPR54 gene as the cause of hypogonadotropic hypogonadism in human subjects.

6. The human clinical data and the murine experimental data disclosed in the attached Exhibits further demonstrate that the GPR54 receptor is required for progression through puberty and that abnormal GPR54 activity results in a sexual disorder. The claimed invention therefore derives a therapeutic utility in that the nucleic acids encoding GPR54 can be used in gene therapy as a means to treat individuals with a sexual disorder (*e.g.*, hypogonadotropic hypogonadism) to increase the expression of this gene in subjects who exhibit reduced or zero expression and activity. Applicants disclose that gene therapy may be used to introduce DNA encoding GPR54 into the cells of target organs and that this procedure would be useful for the treatment of diseases where it is beneficial to elevate GPR54 activity (see page 28, line 9 to 20).

7. I further declare that all statements made herein of my own knowledge are true, and that all statements made on information and belief are believed to be true, and further, that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

March 20th, '06
Date

Brian O'Dowd
Brian O'Dowd, Ph.D.